THE JARED GRANTHAM KIDNEY INSTITUTE NEWSLETTER

A MESSAGE FROM THE DIRECTOR

Welcome to the inaugural newsletter of the Jared Grantham Kidney Institute. The purpose of this newsletter is to keep KUMC and our greater community of supporters, alumni and friends abreast of exciting new developments and accomplishments at the JGKI. At our recent JGKI faculty retreat, I was reminded of the two things that make our Institute special.

Alan Yu, M.B.,B.Chir.

Director, Jared Grantham Kidney Institute

Director, Division of Nephrology and Hypertension, KU School of Medicine

Harry Statland and Solon Summerfield Professor of Medicine, Nephrology and Hypertension

The first is our culture of collegiality and collaboration. Working together, physicians alongside bench scientists, full professors with junior faculty, and kidney scientists with investigators in other disciplines, is simply embedded in our DNA. Two compelling stories in this newsletter exemplify the power of collaboration. On page 6, you will read about Aditi Gupta, who built her career by collaborating with Jeff Burns and the KUMC Alzheimer's Center to study the intersection of chronic kidney disease and cognitive function. The other story tells of how informatics and artificial intelligence expert, Mei Liu, teamed up with myself and a multidisciplinary team to develop a better way to predict acute kidney injury in hospitalized patients.

The second hallmark of the JGKI is the loyalty and support that we have been fortunate to receive from the School of Medicine, the Medical Center, and the community of alumni, friends and supporters in the region and across the country. Through their generosity, we have been able, for example, to award one or more pilot grants each year to provide seed funding for high risk-high reward ideas that are deemed to be unusually innovative and have the potential for a huge impact on kidney disease, but are still in an early developmental stage. Two recent recipients of JGKI pilot grants, Reena Rao and Aditi Gupta, are featured in this issue because their pilot studies blossomed into highly successful projects and garnered extramural funding, in both cases from the National Institutes of Health (NIH).

Indeed, support of our investigators and nascent research projects has proved to be a worthwhile investment. In 2022, the JGKI brought in over $14 million in extramural funding for kidney research, of which $10.4 million was from NIH and DoD awards. So while our annual retreat was focused on planning for the future, let's all take a moment to appreciate just how far we have come, to celebrate our accomplishments to date, and to thank all of our supporters. Rock Chalk, Jayhawk!

JGKI RESEARCH

MICROENVIRONMENT DRIVES CYST GROWTH IN ADPKD

As the most common inherited form of kidney failure, autosomal dominant polycystic kidney disease (ADPKD) affects 1 in every 800 people. Compared to conditions like breast cancer and hypertension, ADPKD is relatively rare, says Reena Rao, Associate Professor of Medicine at the Jared Grantham Kidney Institute.

"But when it's you or your family that is affected by ADPKD, it doesn't seem rare at all," she says.

Dr. Rao has spent the last decade at KUMC and the Jared Grantham Kidney Institute researching ADPKD, trying to better understand the underlying biology of cyst formation to develop new therapies. In 2022, Dr. Rao will receive an R01 grant funded by the National Institutes of Health to investigate how the cyst microenvironment drives cyst growth and scar tissue formation in ADPKD. She has previously been funded by two NIH R01 grants since 2011 to study ADPKD.

Dr. Rao, however, didn't begin her career researching kidney problems. Instead, she received her PhD in food technology in India, which sparked an interest in diabetes. She came to the U.S. for her postdoc training in diabetic kidney damage and happened across a paper on PKD by Jared Grantham himself. This spurred a further evolution of her scientific interests towards vasopressin signaling and PKD.

In the decade since she arrived at KUMC, Dr. Rao has focused her research on cyst formation in ADPKD. As the disease progresses, the large, fluid-filled cysts can take over the kidney. Not only do these cysts cause the kidney to double or triple in volume, but the kidney also developed scar tissue from progressive fibrosis. Together, this disrupts the organ's normal functions, including the removal of toxins and balancing of fluids and electrolytes. As a result, many of those with

"The PKD cyst's microenvironment matters" -Reena Rao, Ph.D.

ADPKD develop kidney failure by the time they're 50. Only one medication, Tolvaptan, is currently approved to help slow cyst growth rate.

With high rates of organ failure and few other treatment options, Rao focused her attention not on the mutation itself but on how the disease progressed. If scientists can figure out a more effective way to halt cyst formation, it might help preserve kidney function for longer in patients with the condition. Just as oncologists have begun to study the tumor microenvironment for clues about why cancer grows and spreads, researchers like Rao have begun to dive into a cyst's surroundings.

"The cyst's microenvironment matters," she says.

The epithelial cells of the cyst wall are surrounded by myofibroblasts, immune cells and extracellular matrix consisting of collagen and other macromolecules. In many other types of diseases, the myofibroblasts main job was producing the extracellular matrix as a way to repair the damaged tissue, a process that results in progressive fibrosis. But when Rao looked more closely at the cysts in people with ADPKD, she found hints that the myofibroblasts had additional jobs. In a mouse model of ADPKD, Rao found

that activation of the vasopressin type-2 receptor in epithelial cells activates myofibroblasts, stimulating them to produce extracellular matrix. Besides identifying a novel biochemical pathway that might provide targets for novel treatments, Rao and colleagues showed that stimulating an epithelial-specific cell signaling pathway might also stimulate myofibroblasts.

To learn more about how epithelial cells and myofibroblasts interacted, Rao co-cultured the two types of cells. When she grew ADPKD epithelial cells with ADPKD myofibroblasts, she found that the cysts formed in culture grew faster and larger compared to ADPKD epithelial cells grown without myofibroblasts. In other words, Rao's work showed that epithelial cells can stimulate myofibroblast accumulation and transform them into a pathogenic cell type. The cross-talk between epithelial and myofibroblast cells creates a positive feedback loop. Vasopressin signaling in ADPKD epithelial cells upregulates and secretes a protein called connective tissue growth factor (CTGF) that is associated with fibrosis and scar tissue formation. CTGF also causes myofibroblasts to become activated and to migrate to sites of cyst formation. The activated myofibroblasts produce additional extracellular matrix, which creates more scar tissue. What's more, the myofibroblasts don't just produce extracellular matrix; they also supply essential nutrients and other factors that induce cell division, thereby paving the way for cyst growth.

Some of the growth factors produced by myofibroblasts bind to receptor tyrosine kinases, proteins that act as an on/off switch for many cellular functions. Nintedanib is a drug that inhibits these kinases and is approved to treat non-small-cell lung cancer, and Rao wanted to know whether it might also help slow cyst growth in ADPKD. In vitro cell culture studies showed that nintedanib reduced the myofibroblast migration and viability, as well as slowing epithelial cell proliferation and cyst growth. Tests in an ADPKD mouse model confirmed these pre-clinical findings, according to results published in Cell Death & Disease.

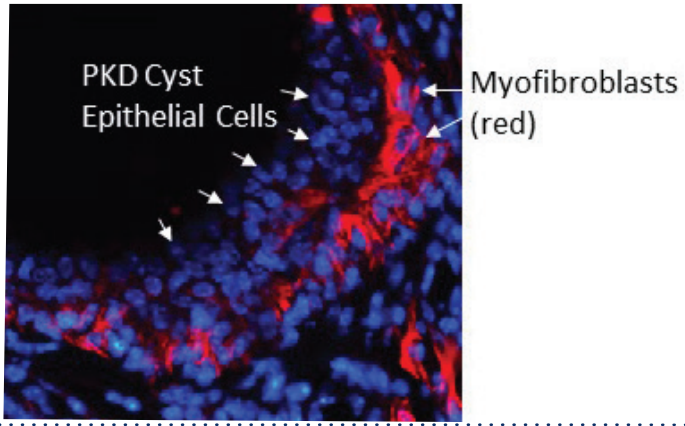
In a new paper published by her group in Kidney International, Rao and collegues have found that reducing the myofibroblasts in the cyst microenvironment can dramatically reduce cyst growth. "This system is very clearly interacting with its microenvironment. We are forgetting that there are other cells that are helping these epithelial cells grow. If we test these cells in isolation, drugs might not work because we haven't considered the cyst microenvironment," Rao says.

Her work is already transforming what scientists think about how cysts form in ADPKD. Instead of being solely determined by the genetic mutations a person carries, kidney cyst formation is also controlled by the environment immediately surrounding the kidney cells. The shift doesn't sound that big, but it's crucial, because it opens up a range of novel ways to target these cysts with pharmaceuticals. And that's where Rao's latest funding comes in.

If she's right, the work will identify a novel way that both cysts and scar tissue form. Kidneys are resilient, Rao points out, and often will continue to function adequately even when they are quite compromised by disease. If scientists can identify ways to keep ADPKD kidneys working long enough, it may prevent the need for dialysis and kidney transplant, Rao says.

Another major goal of hers is to use her lab and research grants to help educate younger scientists about nephrology research. If she can help attract more people to the field, Rao says that there will be more minds focused on kidney health.

"Not many people are interested in the field. So it's important to get another generation of scientists interested in this to keep the research going so that we can really find a proper cure for this disease," Rao says.



USING ARTIFICIAL INTELLIGENCE TO HELP AKI PATIENTS

MEI LIU, PH.D., ALAN YU, M.B., B.CHIR

Acute kidney injury (AKI) is one of the most common complications during hospital stays, affecting one in five adults. The problem is only expected to get worse as the population continues to age and the incidence of conditions like hypertension and diabetes also rises. What makes the issue worse is that physicians don't have good ways to predict which individuals are most likely to develop AKI, which means doctors have little choice but to wait until the problem develops.

To Mei Liu, Ph.D., associate professor of medical informatics in the Department of Internal Medicine at the University of Kansas Medical Center, this sounded like the perfect problem for machine learning. Liu has spent her career using machine learning on electronic health records and big data sets to address healthcare problems. When her colleagues approached her about AKI, she realized it was the perfect problem to tackle with artificial intelligence.

"There are known risk factors, but there are a lot of unknown ones as well, and then there are interactions between these factors. Humans alone can't uncover these relationships, so it's very hard to predict AKI risk," Liu says.

To 'teach' her computer models about how AKI develops and who is most likely to be affected, Liu's team used electronic health record data from 76 957 adult inpatient hospital stays of 2 or more days between 2007 and 2016. At first, Liu created a global model, designed to workbest on a statistically average patient. While the model wasn't terrible, Liu felt she could do better. After all, most patients weren't 'average.' They all deviate from the mean, one way or another. So Liu turned to personalized modeling, where she trained a machine learning model for each incoming patient. Rather than comparing a patient to an artificial average to predict AKI, her model compared them to a group of similar patients.

The shift made a big difference, according to results published in July in JAMA Network Open. Liu's personalized model learned more quickly and was more accurate than her previous global models, performing an average of 4% to 5% better. In some subgroups, such as high-risk patients undergoing liver and cardiac surgeries, the personalized model performed as much as 13% better. It might not sound like much, Liu admits, but because so many hospitalized adults develop AKI, even a small reduction would make a difference to many patients.

Unlike many other machine learning approaches, which don't reveal the factors contributing to the increased risk of AKI, Liu's model allows clinicians to see which variables are increasing risk, and by how much. Together with nine other research sites, Liu's team has begun a deep dive into the 'unknown' risk factors increasing AKI in her models to gain a better understanding of what is driving the problem. Liu hopes that her model will one day be adopted as a clinical decision support tool that will create an alert for those patients at the highest risk of AKI.

Watch on YouTube: Mei Liu and Alan Yu talk about using artificial intelligence prediction models for acute kidney injury on Open Mic with Dr. Stites

JGKI RESEARCH

THE BRAIN-KIDNEY AXIS

Dialysis is hard on every organ system. While its impact on the cardiovascular system is well documented, Associate Professor Aditi Gupta found little information about how dialysis affected neurocognition. As a transplant nephrologist, Gupta watched as many of her patients reported an increasing brain fog as they remained on dialysis. When they received a transplant, however, their issues with cognition and memory vanished.

At first, Gupta chalked that up to the benefits of transplant. Then she began to wonder whether dialysis was having a negative impact on brain functioning, and whether she could do something about it.

As early as the 1930s, scientists had noticed a link between chronic kidney disease (CKD) and encephalopathy. But almost a century later, no one could say for sure what caused the vascular disease and white matter changes that appeared on MRI scans. Part of what makes answering that question complicated is that chronic kidney disease rarely occurs on its own. Patients frequently have co-occurring conditions such as diabetes, hypertension, and heart disease, which can make it hard to determine whether kidney disease is causing cognitive impairment on its own, and how these other conditions contribute. And these neurological problems also impacted patients' kidney health. A 2019 study in CJASN showed that dialysis patients with cognitive impairment were less likely to be on the transplant list and spent more time waiting when they were.

Gupta began her investigations with a small pilot grant from the Jared Grantham Kidney Institute in 2013, and she has since developed into a fully-fledged clinician-researcher with major NIH grants.

"The big question is, can we prevent this from happening?" -Aditi Gupta, M.D

To figure out how kidney disease impacts the brain, Gupta is taking an unusual tack: she's studying what domains of cognition improve post-transplant. Her work is focusing on three major brain alterations seen in CKD patients, such as changes to cerebral blood flow, alterations in neurochemicals, and a disruption to the brain's connective white matter. Since these issues persist even through dialysis, Gupta wanted to figure out if and how they normalized after transplant.

Together with neurologist Jeffrey Burns, Gupta recruited 29 patients with ESRD between the ages of 30 and 70, as well as 19 healthy controls. The researchers compared brain scans taken pre-transplant, and 3- and 12-months post-transplant. Results showed that blood flow to the brain dropped after transplant to levels seen in controls. Magnetic resonance imaging revealed that levels of two neurochemicals, choline and myo-inositol, which were increased in ESKD patients before transplant, decreased after transplant. White matter connections between neurons also normalized, as detailed in a 2021 study in JASN.

Gupta suspects these factors normalize with transplant rather than dialysis because dialysis does not remove blood toxins like a kidney does. Those toxins, in turn, damage the blood-brain barrier. As a result, she says, harmful molecules that normally cannot enter the brain, can now gain entry inside the brain tissue.

FACULTY NEWS

ACADEMIC PROMOTION & TENURE

Effective July 1, 2022
Reem Mustafa, M.D., Ph.D., MPH
Professor

FACULTY AWARDS

Pam Tran, Ph.D.
Rising Trendsetter 2022 STEMMy Award from Central Exchange

Akinlolu Ojo, M.D., Ph.D., MBA
Elected to the National Academy of Medicine

Alan Yu, M.B. B.Chir.
KUMC Internal Medicine Outstanding Investigator Award, 2022

JGKI COMMITTEE LEADERS

Join us in thanking our faculty for their leadership of our JGKI Committees:

Research Collaborations
Drs. Stephen Parnell, Jason Stubbs, Madhulika Sharma

Work Force/Mentoring
Drs. Reena Rao, Darren Wallace, Pamela Tran

Funding Sources
Drs. Chris Ward, Darren Wallace, Alan Yu

Research Support
Drs. Kelly Liang, Robin Maser, James Calvet

New and Diverse Science
Drs. Aditi Gupta, Dale Abrahamson, Madhulika Sharma, Robin Maser

Visibility of our Work
Drs. Alan Yu, Pamela Tran, Reem Mustafa, James Calvet

PKD CENTER LEADERSHIP

Darren Wallace, Ph.D., became the PKD Center Director and PI of our PKD U54 in July. We are grateful to **James Calvet, Ph.D.**, for his outstanding center leadership from 2005-2022.

WELCOME NEW FACULTY

Emmanuel Adomako, MB, ChB
Assistant Professor
Nephrology and Hypertension
Interests include mineral metabolism (including kidney stones) and electrolyte physiology.

Kelly V. Liang, MD
Associate Professor
Nephrology and Hypertension
Research interests in lupus nephritis, cardiorenal failure, acute kidney injury, and nephrolithiasis. She has done several retrospective studies in biomarkers for lupus nephritis with correlation to biopsy findings.

Kyle Jansson, MD, PhD
Assistant Professor
Nephrology and Hypertension
Research interest is in the role of phosphaturia in mechanisms of kidney injury and inflammation in CKD.

PUBLICATIONS

FACULTY REPORTED PUBLICATIONS

James Calvet:

Prdx5 regulates DNA damage response through autophagy-dependent Sirt2-p53 axis. Agborbesong E, Zhou JX, Li LX, Harris PC, Calvet JP, Li X. Hum Mol Genet. 2022 Sep 6:ddac218. doi: 10.1093/hmg/ddac218. Online ahead of print.PMID: 36067023

The Ionidamine derivative H2-gamendazole reduces cyst formation in polycystic kidney disease.Sundar SV, Zhou JX, Magenheimer BS, Reif GA, Wallace DP, Georg GI, Jakkaraj SR, Tash JS, Yu ASL, Li X, Calvet JP. Am J Physiol Renal Physiol. 2022 Oct 1;323(4):F492-F506. doi: 10.1152/ajprenal.00095.2022. Epub 2022 Aug 18.PMID: 35979967

Aditi Gupta:

Implementing a home-based virtual hypertension program-A pilot feasibility study. Family Practice. Aug 2022. Gupta, Aditi; Ellis, Shellie D.; Burkhardt, Crystal; Young, Kate; Mazzotti, Diego R.; Mahnken, Jonathan; Abu-el-rub, Noor; Chandaka, Sravani; Comfort, Branden; Shanks, Denton; Woodward, Jennifer; Unrein, Amber; Anderson, Heidi; Loucks, Jennifer; Song, Xing; Waitman, Lemuel R.; Burns, Jeffrey M. (Corresponding author)

Pre-transplant psoas muscle cross-sectional area and post-kidney transplant outcomes. Transplant Proceedings 2022. Taylor Norris, Robert Montgomery, Diane Cibrik, Mark Reintjes, Shweta Chakraborty, Shelby Fishback, Aditi Gupta. (Senior Corresponding author)

Pre-transplant cognitive screening is a poor predictor of post-transplant cognitive status. Gupta A, Montgomery RN, Young K, Mukherjee R, Chakraborty S, Thomas TS, Cibrik DM, Drew D, Sarnak M. Clin Transplant. 2022 Aug 21;:e14798. doi: 10.1111/ctr.14798. [Epub ahead of print] PubMed PMID: 35989467.

Insights into Cognitive Brain Health in Chronic Kidney Disease. Tariq H, Ramakrishnan M and Gupta A. Gerontology and Geriatrics: Research. 2022 August; 8(2). (Senior Corresponding author)

Heterogeneous cardiovascular profiles in CKD: ADPKD Versus non-ADPKD. Aug 2022, Kidney International Reports. Eric Au, Aditi Gupta. (Senior Corresponding author)

Stephen Parnell:

Drs. Maser, Calvet, and Parnell published a review article entitled The GPCR Properties of Polycystin-1 -- A New Paradigm (to be published as a part of Frontiers Molecular Biosciences review series “Molecular Mechanisms Underlying Polycystic Kidney Disease: From the Smallest Bricks to the Big Scenario

Kidney stone formation in a novel murine model of polycystic kidney disease. Riddle HAL, Zhang S, Qian F, Williams JC Jr, Stubbs JR, Rowe PSN, Parnell SC. Am J Physiol Renal Physiol. 2022 Jul 1;323(1):F59-F68. doi: 10.1152/ajprenal.00165.2021. Epub 2022 Mar 28. PMID: 35343849

PUBLICATIONS - CONTINUED

Reem Mustafa:

Systematic Review of Reported Outcomes in ADPKD Studies. Jdiaa SS, Husainat NM, Mansour R, Kalot MA, McGreal K, Chebib FT, Perrone RD, Yu A, Mustafa RA. A Kidney Int Rep. 2022 Sep;7(9):1964-1979. doi: 10.1016/j.ekir.2022.06.012. eCollection 2022 Sep. PubMed PMID: 36090492; PubMed Central PMCID: PMC9459055.

A Framework for the Development of Living Practice Guidelines in Health Care. El Mikati IK, Khabsa J, Harb T, Khamis M, Agarwal A, Pardo-Hernandez H, Farran S, Khamis AM, El Zein O, El-Khoury R, Schünemann HJ, Akl EA, Alonso-Coello P, Alper BS, Amer YS, Arayssi T, Barker JM, Bouakl I, Boutron I, Brignardello-Petersen R, Carandang K, Chang S, Chen Y, Cuker A, El-Jardali F, Florez I, Ford N, Grove J, Guyatt GH, Hazlewood GS, Kredo T, Lamontagne F, Langendam MW, Lewin S, Macdonald H, McFarlane E, Meerpohl J, Munn Z, Murad MH, Mustafa RA, Neumann I, Nieuwlaat R, Nowak A, Pardo JP, Qaseem A, Rada G, Righini M, Rochwerg B, Rojas-Reyes MX, Siegal D, Siemieniuk R, Singh JA, Skoetz N, Sultan S, Synnot A, Tugwell P, Turner A, Turner T, Venkatachalam S, Welch V, Wiercioch W. Ann Intern Med. 2022 Aug;175(8):1154-1160. doi: 10.7326/M22-0514. Epub 2022 Jul 5. Review. PubMed PMID: 35785533.

Laboratory assays of VWF activity and use of desmopressin trials in the diagnosis of VWD: a systematic review and meta-analysis. Kalot MA, Husainat N, Abughanimeh O, Diab O, El Alayli A, Tayiem S, Madoukh B, Dimassi A, Qureini A, Ameer B, Eikenboom J, Giraud N, Haberichter S, Jacobs-Pratt V, Konkle BA, McRae S, Montgomery R, O'Donnell JS, Brignardello-Petersen R, Flood V, Connell NT, James P, Mustafa RA. Blood Adv. 2022 Jun 28;6(12):3735-3745. doi: 10.1182/bloodadvances.2021005431. PubMed PMID: 35192687.

Outcomes of long-term von Willebrand factor prophylaxis use in von Willebrand disease: A systematic literature review. El Alayli A, Brignardello Petersen R, Husainat NM, Kalot MA, Aljabiri Y, Turkmani H, Britt A, El-Khechen H, Shahid S, Roller J, Motaghi S, Mansour R, Tosetto A, Abdul-Kadir R, Laffan M, Weyand A, Leebeek FWG, Arapshian A, Kouides P, James P, Connell NT, Flood VH, Mustafa RA. Haemophilia.2022 May;28(3):373-387. doi: 10.1111/hae.14550. Epub 2022 Mar 26. Review. PubMed PMID: 35339117.

Current State of Evidence on Kidney Transplantation: How Fragile Are the Results?. Budhiraja P, Kaplan B, Kalot M, Alayli AE, Dimassi A, Chakkera HA, Heilman R, Edwards AS, Mustafa RA. Transplantation. 2022 Feb 1;106(2):248-256. doi: 10.1097/TP.0000000000003805. PubMed PMID: 33966022.

Reena Rao:

Vasopressin Receptor Type-2 Mediated Signaling in Renal Cell Carcinoma Stimulates Stromal Fibroblast Activation. Jamadar A, Dwivedi N, Mathew S, Calvet J, Thomas S and Rao R.. Int. J. Mol. Sci. 2022 July; 23(14):7601, PMC9325308, PMID: 35886951.

Myofibroblast depletion reduces kidney cyst growth and fibrosis in autosomal dominant polycystic kidney disease. Dwivedi N, Jamadar A, Mathew S, Fields TA, Rao R. Kidney Int. 2022 Oct 20;S0085-2538(22)00841-9. PMID

Jason Stubbs:

Correction of Vascular Calcification and Hyperphosphatemia in Chronic Kidney Disease Rats Treated with ASARM peptide. Peter S. Rowe, Ellen M. McCarthy, Alan L. Yu and Jason R. Stubbs Kidney360 August 2022, 10.34067/KID.0002782022;

Critical Role of Osteopontin in Maintaining Urinary Phosphate Solubility in CKD. Jason R. Stubbs, Shiqin Zhang, Kyle P. Jansson, Timothy A. Fields, Joseph Boulanger, Shiguang Liu and Peter S. Rowe. Kidney360 September 2022, 3 (9) 1578-1589;

PUBLICATIONS - CONTINUED

Pamela Tran:

Genetic Interaction of Thm2 and Thm1 Shapes Postnatal Craniofacial Bone. Bumann EE, Hahn Leat P, Wang HH, Hufft-Martinez BM, Wang W, Tran PV. J Dev Biol. 2022 May 11;10(2):17. doi: 10.3390/jdb10020017. PMID: 35645293

Mitochondrial pharmacotherapy during pregnancy and lactation in an ADPKD mouse model: a win for both mothers and their offspring. Wang W, Tran PV. Kidney Int. 2022 May;101(5):870-872. doi: 10.1016/j.kint.2022.02.008. PMID: 35461611

Ttc21b deficiency attenuates autosomal dominant polycystic kidney disease in a kidney tubular- and maturation-dependent manner. Wang W, Silva LM, Wang HH, Kavanaugh MA, Pottorf TS, Allard BA, Jacobs DT, Dong R, Cornelius JT, Chaturvedi A, Swenson-Fields KI, Fields TA, Pritchard MT, Sharma M, Slawson C, Wallace DP, Calvet JP, Tran PV. Kidney Int. 2022 Sep;102(3):577-591. doi: 10.1016/j.kint.2022.04.034. Epub 2022 May 27. PMID35644283

Darren Wallace:

PKD1 and PKD2 mRNA cis-inhibition drives polycystic kidney disease progression. Lakhia, R, H. Ramalingam, C.M. Chang, P. Cobo-Stark, L. Biggers, A. Flaten, T. Valencia, D.P. Wallace, E.C. Lee, and V. Patel. Nat. Commun. 13(1): 4765, 2022.

CaMK4 overexpression in polycystic kidney disease promotes mTOR-mediated cell proliferation. Zhang, Y., E.A. Daniel, J. Metcalf, Y. Dai, G.A. Reif, and D.P. Wallace. J. Mol Cell Biol, Aug 24 (Online ahead of print), 2022.

Ttc21b deficiency attenuates autosomal dominant polycystic kidney disease in a kidney tubular- and maturation-dependent manner. Wang W, L.M. Silva, H.H. Wang, M.A. Kavanaugh, T.S. Pottorf, B.A. Allard, D.T. Jacobs, R. Dong, J.T. Cornelius, A. Chaturvedi, K.I. Swenson-Fields, T.A. Fields, M.T Pritchard, M. Sharma, C. Slawson, D.P. Wallace, J.P. Calvet, and P.V. Tran. Kidney Int. 102(3):577-591, 2022.

The lonidamine derivative H2-gamendazole reduces cyst formation in polycystic kidney disease. Sundar, S.V., J.X. Zhou, B.S. Magenheimer, G.A. Reif, D.P. Wallace, G.I. Georg, S.R. Jakkaraj, J.S. Tash, A.S.L. Yu, X. Li, and J.P. Calvet. Am J Physiol Renal Physiol. 323(4): F492-F506, 2022.

Expression of active B-Raf proto-oncogene in kidney collecting ducts induces cyst formation in normal mice and accelerates cyst growth in mice with polycystic kidney disease. Parnell, S.C., A. Raman, Y. Zhang, E.A. Daniel, Y. Dai, A. Khanna, G.A. Reif, J.L. Vivian, T.A. Fields, and D.P. Wallace. Kidney Int. 102(5): 1103-1114, 2022.

Alan Yu:

Development and validation of a personalized model with transfer learning to estimate acute kidney injury using electronic health records of hospitalized patients. Liu K, Zhang X, Chen W, Yu ASL, Kellum JA, Matheny ME, Simpson SQ, Hu Y, Liu M. JAMA Netw Open, in press

Correction of vascular calcification and hyperphosphatemia in rats treated with ASARM peptide. Rowe PS, McCarthy EM, Yu ASL, Stubbs JR. Kidney 360, in press

RECENT GRANTS & CONTRACTS

NEW SINCE MAY 2022

ADITI GUPTA, MD, MS

K23 Supplement for Cognitive Impairment in End Stage Renal Disease
NIA

REENA RAO, PH.D.

Pathogenic reciprocal interplay between cyst epithelium and myofibroblasts in polycystic kidney disease.
NIH/NIDDK. 1R01DK135308-01, Rao, Reena (PI).

The Role of Circadian Rhythm Disruption in Polycystic Kidney Disease Progression.
Department of Defense Discovery Award, Rao, Reena (PI).

Pilot and feasibility grant: V2R-HIF1α-CCL20 mediated tumor cell regulation of CAFs in ccRCC.
Internal - KUMC Cancer Center and Kidney Institute

MADHULIKA SHARMA, PH.D.

Inflammatory roles of ferritin in polycystic kidney disease
Polycystic Kidney Disease Foundation

PAMELA TRAN PH.D.

Pilot and feasibility grant: Mechanisms of micrognathia in a ciliopathy mouse model of osteochondrodysplasia.
Bionexus KC Patton Trust
Co-PI is Erin Bumann from UMKC

ALAN YU, M.B., B.CHIR.

Therapeutic Development Award: Development of 2-deoxy-D-glucose for the treatment of polycystic kidney disease (Subcontract PI)
Prime: Ospedale San Raffaele
Department of Defense Technology

Developmental Project Award: Role of blood brain barrier disruption in cognitive dysfunction
Internal: University of Kansas Alzheimer's Disease Research Center

CLINICAL TRIALS

KELLY V. LIANG, MD

A Study of the Prevalence of Apolipoprotein L1 (APOL1) Alleles Among Individuals With Proteinuric Kidney Disease Who Are of Recent African Ancestry or Geographic Origin
Clinical Trial Sponsor: Vertex

A Phase 2/3 Adaptive, Double-blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of VX-147 in Subjects Aged 18 Years and Older With APOL1-mediated Proteinuric Kidney Disease (AMPLITUDE)
Clinical Trial Sponsor: Vertex

A Prospective Observational Registry of Patients Treated with LUPKYNIS™ (voclosporin) in the US (ENLIGHT)
Clinical Trial Sponsor: Aurinia

ELLEN MCCARTHY, MD

Nephrotic Syndrome Network (NEPTUNE)
The NEPTUNE cohort study is a prospective, observational study that enrolls children and adults with FSGS, MCD, and MN
Sponsor: NIDDK, Prime: University of Michigan

Our institute faculty have received over $10 million of grant support this year from NIH and DoD

TRAINEE NEWS

Anubhav Chakraborty, PhD student (Mentor: Alan Yu)
Anubhav had an ASN abstract accepted for poster presentation on"*Early Cyst formation leads to the development of an inflammatory microenvironment and tissue remodeling in polycysic kidney disease*"

Johnny Dinh Phan, K-INBRE scholar (Mentor: Madhulika Sharma)
Johnny presented a poster at ASN on "*Ferritin as an inflammatory molecule in Autosomal Dominant Polycystic Kidney Disease"*

Emily Daniel, a well-trained and highly motivated Research Assistant mentored by Darren Wallace, has joined the Interdisciplinary Graduate Program in Biomedical Sciences (IGPBS) program as a PhD student at KUMC.

Abdallah El Alayli, Postdoctoral Fellow (Mentor: Reem Mustafa)
Abdallah presented two posters and one oral presentation at the SGIM Midwest regional meeting in October 2022. The posters were summarizing reviews done by members of the Outcome and Implementation Research Unit to inform the World Health Organization (WHO) pharmacological treatment guidelines.

Ibrahim El Mikati, Postdoctoral Fellow (Mentor: Reem Mustafa)
Ibrahim received the Evidence Foundation Scholar award based on project that aims helping to develop guidance for judging imprecision in diagnostic evidence in June 2022. He also received the KUMC Post-doctoral Association travel award.

Abeda Jamadar, Postdoctoral Fellow (Mentor: Reena Rao)
Abeda presented a poster at ASN on "*The Renal Circadian Clock is Disrupted in Autosomal Polycystic Kidney Disease"*

Matthew Kavanaugh, MD-PhD student (Mentor: Pamela Tran)
Matthew received a Drs. Ash Scholarship (pays $2500 for tuition). He also had an ASN abstract chosen for oral presentation at 2022 Kidney Week on *"Downregulation of O-GlcNAc reduces ciliary length and attenuates renal cystic disease in PKD mice"*

Brittany Martinez, PhD student (Mentors: Pamela Tran and Irfan Saadi)
Brittany's abstract on "*SPECC1L deficiency causes shortened primary cilia and genetically interacts with IFT-A deficiency to affect palatogenesis"* was chosen for oral presentation at the 2022 Society for Craniofacial Genetics and Developmental Biology meeting

Dr. Yan Zhang, Postdoctoral Fellow (Mentor: Darren Wallace)
Accepted a faculty position as Research Assistant Professor at the Michigan Technological University. Yan will have an adjunct faculty position in the JG Kidney Institute.

SPECIAL PROGRAMS

PKD CENTER HOSTS SUMMER STUDENTS

The JGKI's PKD Center hosted 8 summer scholars as part of our U54 funded Summer Student Enrichment Program. The program partnered students with a PKD Center faculty mentor to become immersed in a polycystic kidney disease related research project for a full-time, ten-week period over the summer.

Aarya Bestha, KU Sophmore, Mentor: Jason Stubbs
Aakriti Chaturvedi, KU Senior, Mentor: Pamela Tran
Kilee Hale, KU Freshman, 5/30-8/10, Mentor: Alan Yu
Mercedes McGonigle, KU Senior, Mentor: Madhulika Sharma
Mary Parnell, Oklahoma State Junior, Mentor: Stephen Parnell
Noah Schneiders, KU Senior, Mentor: Robin Maser
Jad Shawa, High School Senior, Mentor: Chris Ward
Olivia Robison, KU Senior, Mentor: Darren Wallace

RIDE FOR PKD VISIT

Glenn Frommer, who has polycystic kidney disease (PKD), rode his bicycle cross-country this summer to raise awareness and funds for PKD research. He stopped in Kansas City on July 7th to meet researchers, staff and students at the Jared Grantham Kidney Institute. The cyclist talked about his goals for the ride, and then Kidney Institute scientists opened their labs and shared about our ongoing research. Mr. Frommer completed his ride in September and raised over $585,000.

VISITING SCHOLAR: DR. SEVCAN BAKKALOGLU

During the month of August, Dr. Sevcan Bakkaloglu, Professor of Pediatrics and Head of the Department of Pediatric Nephrology and Rheumatology at Gazi University, Faculty of Medicine in Ankara-Turkey visited the Outcomes and Implementation Research Unit. She had hands on experience with the development of evidence-based guidelines using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology. She worked on evidence synthesis to inform the diagnosis and treatment guidelines for catheter-related infections in pediatrics peritoneal dialysis.

For more on JGKI programs, events and visiting scholars, follow our **Twitter @KUJGKI: twitter.com/KUJGKI**

GRANTHAM SYMPOSIUM

JARED J GRANTHAM SYMPOSIUM: THE FUTURE OF PKD RESEARCH

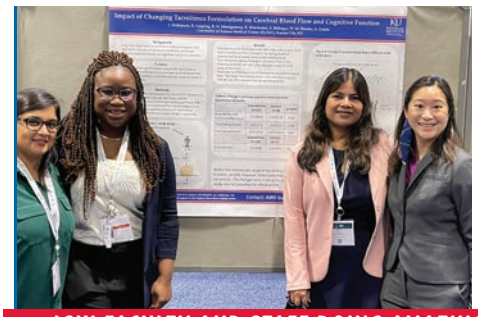
To honor Dr. Jared Grantham in his retirement, we hosted the first Jared J. Grantham Symposium in 2014 in Kansas City. Dr. Grantham's vision was to invite all of the Lillian Jean Kaplan award recipients to lead a forward-thinking and interactive forum to focus on future directions and innovations in polycystic kidney disease research. All twelve of the Kaplan Awardees were present at the inaugural symposium to give talks on their vision of " The Future of PKD Research." The Kidney Institute continues to host the Grantham Symposium annually. Over 100 researchers attended the online symposium this year that was held on June 10, 2022. The recent Kaplan Awardees were the keynote speakers at this year's symposium:

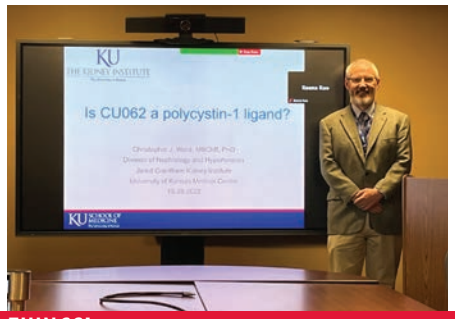
Alessandra Boletta, Ph.D.
Head, Molecular Basis of Cystic Kidney Disorders Unit
Division of Genetics and Cell BiologySan Raffaele Scientific Institute, Milan, Italy
"Metabolic Reprogramming in Polycystic Kidney Disease"

Albert Ong, DM, MA, FRCP
Professor of Renal Medicine and Head, Academic Nephrology
Department of Infection, Immunity and Cardiovascular Disease
University of Sheffield Medical School, United Kingdom
"Understanding Biological Variation in ADPKD: Lessons from Nature"

Arlene Chapman, M.D.
Professor of Medicine and Chief, Section of Nephrology
Director, Clinical Research Center, Institute for Translational Medicine
University of Chicago Medical Center
"***ADPKD - Membership in the Cysterhood"***

PHOTO GALLERY

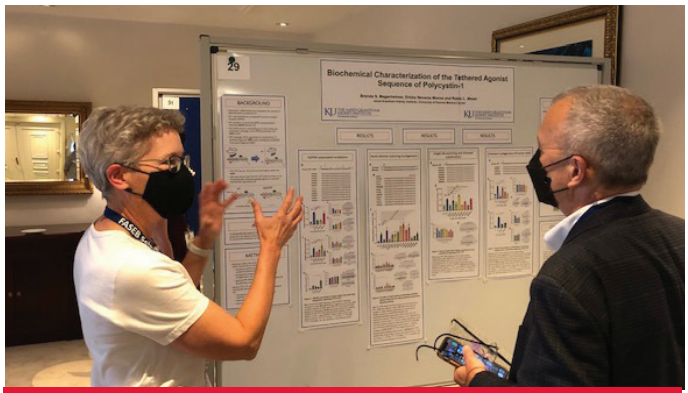




JGKI FACULTY AND STAFF DOING AMAZING THINGS!

JGKI SUMMER STUDENTS, DR. MUSTAFA PRESENTING, YU LAB

PHOTO GALLERY



BRENDA MAGENHEIMER - FASEB POSTER

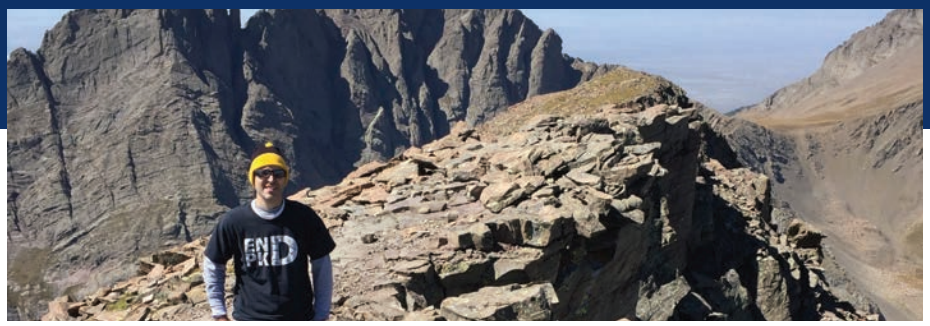
HONORING DR. CALVET: PAINTING BY BRENDA MAGENHEIMER

DR. YU RECEIVING OUTSTANDING INVESTIGATOR AWARD

TEAM RENAL AVENGERS AT THE WALK FOR PKD

SIGHTSEEING IN LISBON DURING FASEB

ROBIN AND DARREN AT FASEB IN LISBON



JGKI FACULTY AND STAFF DOING AMAZING THINGS!

LEFT: RENAL TRANSPLANT TEAM | RIGHT: OUTCOMES RESEARCH UNIT AT TOPGOLF | BOTTOM RIGHT: NKF WALK BOOTH

UPCOMING EVENTS

THE JARED GRANTHAM
KIDNEY INSTITUTE
NEWSLETTER

JGKI HOLIDAY PARTY

FRIDAY, DECEMBER 2, 2022

7:00-10:00PM

Chicken and Pickle
5901 W. 135th St
Overland Park 66223

SHARE YOUR NEWS!

Please send your news and photos to be included in the next newsletter to Lyn Harris, lharris3@kumc.edu.